Blood Lead Modeling Meeting
January 18, 2018
AGENDA and HANDOUT

1. Overview/Introductions- Charles Bevington (OPPT)
2. Initial overview of IEUBK- Michele Burgess (OLEM)
3. Initial overview of AALM- James Brown (ORD)
4. Status of cross-office peer review – Charles Bevington (OPPT)

Overview/Introductions-Charles Bevington

Cross-Office Coordination and Collaboration to update Blood Lead Models

Important considerations when updating Blood Lead Models

Exposures

Lead exposure occurs via both inhalation and ingestion of Pb from various media: soil, dust, air, drinking water, food, paint, other sources

Uptake

Absorption of Lead from contaminated media is informed by:

- Age specific exposure factors
- Media specific bioavailability

Biokinetics

Disposition of Lead throughout the body is informed by:

- Age specific compartment volumes (blood, bone, tissue)
- Age and compartment-specific rates of transfer between these compartments over time

AALM	IEUBK Model
Can simulate highly intermittent and short term exposures for any age, with a minimum exposure averaging time of 1 day	Simulates quasi-steady state exposures (minimum averaging time of 3 months to 1 year) in young children (0 – 84 months)
Can evaluate intermittent or steady state exposures. Outputs Pb concentrations in blood, plasma, bone, soft tissues (including kidney and liver) and excreta	Can evaluate numerous steady state exposures scenarios. Outputs only blood Pb concentrations
AALM implements a multi-compartmental PBPK model in children and adults (0 – 90 years)	IEUBK implements a multi-compartmental PBPK model only for children up to age 7 (84 months)
Recent updates focus on uptake and biokinetics.	Recent updates focus on exposure and uptake.

IEUBK Overview- Michele Burgess

The Office of Land and Emergency Management (OLEM), Office of Superfund Remediation & Technology

Innovation (OSRTI), Technical Review Workgroup for Lead (TRW) updates to the Integrated Exposure Uptake Biokinetic Model (IEUBK).

Since 1994, OLEM risk assessments for lead in residential settings at Superfund sites utilize the IEUBK model, using a child as the receptor.

The IEUBK model is a multi-media model that predicts blood lead concentrations in children from environmental lead exposures.

History of Independent Reviews of the IEUBK:

- 1990 EPA Science Advisory Board (SAB) review for NAAQS
- 1992 SAB review and External Peer Review of IEUBK
- 1998 Independent Validation and Verification
- 1998 SAB review for TSCA Section 403 Regulation
- 2005 National Academy of Sciences (NAS) review for Coeur d' Alene site report

In 2010, the TRW initiated review of IEUBK default input parameters for an update based on more recent science. The default parameters that were reviewed are the following: dietary lead, water consumption, water concentration, inhalation rate, relative bioavailability and soil/dust ingestion rate.

The recommendations (with the exception of soil/dust ingestion rate) for updating the parameters underwent peer review in 2013 and OSRTI management review in 2017

The soil/dust ingestion rate was peer reviewed in 2017, and OSRTI is adjudicating comments to finalize the parameter.

The updated default input parameters will be used to build version 2 of the IEUBK model. OSRTI expects to update the IEUBK defaults in 2018.

- Ventilation rate. Current is 2–7 m^3/day (age-specific), proposed is 3.22 – 8.89 m3/day (age-specific) based on energy expenditure from Institute of Medicine's doubly-labeled water dataset and equations developed (Brochu et al. 2006 and Layton, 1993) to convert metabolic energy to inhalation rates
- Dietary lead exposure. Current is ~2–2.3 µg/day (age-specific), proposed is ~2.7–6.0 µg/day (age-specific) based on new FDA food residue information and National Cancer Institute food consumption analysis
- Bioavailability. Current is 60% RBA and proposed is the same based on analysis of the full data set of site-specific lead bioavailability studies
- Water Consumption. Current is 0.2–0.59 L/day (age-specific). Proposed is 0.4–0.63 L/day (age-specific) based on Kahn and Stralka, 2009 (All Water Sources, Consumers Only)
- Soil and Dust Ingestion Rate. Current is 85-135 mg/day (age-specific). Proposed draft information suggests ~62 mg/day (age-specific) based on information from Bunker Hill Superfund Site in Idaho and other studies
- Water Lead Concentration. Current is 4 ppb. Proposed is 0.9 ppb based on population-weighted estimate from Office of Water 6-year lead and copper rule data set

OSTRI Plans to incorporate and adjudicate the soil/dust ingestion rate default input parameter, evaluate the IEUBK model to compare blood lead predictions with updated defaults against available data. OSTRI also plans to obtain OSRTI Office Director signature of the updated IEUBK variables and continue to brief OLEM management.

AALM Overview- James Brown

The All Ages Lead Model (AALM) estimates the effect of lead exposures from various media (air, water, food, dust, and soil) on lead concentrations in blood and various other tissues from infancy through adulthood up to 90 years of age.

The precursor to the AALM is EPA's Integrated Exposure Uptake Biokinetic (IEUBK) Model for lead in children less than 7 years old.

ORD/NCEA-RTP and OCSPP/OPPT have coordinated efforts to advance the AALM since FY2016. The AALM accounts for the internal disposition of lead at any age for specified exposures (acute and/or chronic).

A Microsoft Excel user interface allows risk assessors to specify detailed exposure scenarios (e.g., duration of exposures and levels of lead in in various media). An exposure scenario is run via an Excel macro and results are returned to Excel for review or further analysis. This capability facilitates risk assessment decisions.

Current efforts aim to have the AALM peer-reviewed in FY2018. Four documents that will be subject to peer-review are described below.

1) AALM Fortran Users Guide (anticipated February 2018; apx. 20 pages) – This document describes software installation and provides instructions for the Excel user interface.
2) Theoretical Framework for the All Ages Lead Model (anticipated February 2018; apx. 40 pages of text with equations) – This document provides a brief history to the AALM and the three software platforms (Fortran, acslX, and visual C) in which it has been implemented. The primary focus of Sections 4 and 5 is to explicitly describe the Fortran implementation and equations used as part of this version. The document includes several tables, figures, and additional appendices:
    a. Tables (3) for exposure equations, biokinetic and growth equations, rate constants
    b. Figures (4) illustrating model structure and gastrointestinal absorption
    c. Appendix A – Equations for the AALM Fortran (23 pages, generally repeats tables noted above in Item 2a)
    d. Appendix B – Description of AALM Fortran Parameters (27 pages)
    e. Appendix C – AALM Fortran Exposure Parameter Values (21 pages)
3) Evaluation of the Fortran Version of the All Ages Lead Model (November 2016; 30 pages, 6 tables, 24 figures) – This document describes the comparison of an Advanced Continuous Simulation Language (acslX) and Fortran implementation of the AALM. The process of harmonizing the two model versions, evaluating the differing biokinetics for the two versions against available human data, and selection of final model parameters are provided.
4) Evaluation and Development of the AALM (October 2014; 25 pages, 22 tables, 28 figures) – This document provides a sensitivity analysis of model parameters for an acslX implementation of the model. An evaluation and optimization of the Leggett and O'Flaherty biokinetics models against a common set of observations is described. A biokinetic parameter controlling Pb binding to red blood cells Pb concentrations was adjusted to align the AALM results more closely with the IEUBK model for children without adversely impacting the good model agreement and predictive capability for infants or adults.

An additional three background documents will be available to the peer-reviewers that describe prior work on the Visual C implementation on the AALM completed over the period of 2007-2009; these background documents will not be subject to peer-review.

1) Guidance Manual for the AALM that describes the conceptual basis and structure of the model (including all equations, parameters, and parameter values). This is updated by Item 2 above.
2) Review and evaluation of evidence supporting extension and/or refinement of the AALM
3) Review of biokinetics models for lead in children and adults

Cross-Office Peer Review- Charles Bevington

Options are available for peer review of Blood Lead Models. Both of these models have been peer reviewed in the past. Peer review options include: contractor led, panel, letter with consultation, and letter.

Funds have been set aside from multiple offices to support peer review and Office of Water is providing FTE support to manage the process.

Key Tasks and Milestones for a Contractor-Managed Peer Review of EPA HISA and ISI products. Peer review of AALM is very likely HISA.

- FR Notice 1 – solicit peer reviewer nominations and initiate public comment period of product
- FR Notice 2 – comment period for interim list of peer reviewers
- FR Notice 3 – announces the final peer reviewers, charge questions, and public peer review meeting logistics
- Public review panel meeting
- Final peer review report

Task Name	**Duration (days)**
Contract vehicle in place (Task order or work assignment), compete if task order	15-45
Initiate Task; Develop Schedule and FR Notice 1; Open Docket	15-30
45-day Peer Reviewer Nomination Period and Public Comment Period (FR Notice 1)	**45**
Review Qualifications and Conduct COI (FR Notice 1)	7-14
Submit Interim list and FR Notice 2 for EPA review	7-14
21-Day Interim List Comment Period for Panel (FR Notice 2)	**21**
Select Final Reviewers for Panel (including meeting with Science Advisor)	7-14
Pre-Meeting Arrangements and FR Notice 3 for Panel (Final Reviewers, Meeting Notice, Charge)	**7**
Meeting Registration Period; Peer Reviewer Period for Final Reviewers	15-30
In Person Public Review Panel Meeting	1-2
Post Meeting Arrangements (Final Report)	**30**
Total Duration	6 to 9 months